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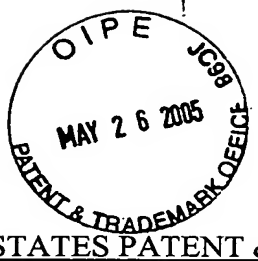


DOCKET NO: 271120US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
NAOKI MATSUNAGA, ET AL.	: EXAMINER:
SERIAL NO: 10/532,104	:
FILED: APRIL 21, 2005	: GROUP ART UNIT:
FOR: N-{2-CHLORO-4-[(6,7-DIMETHOXY -4-QUINOLYL)OXY]PHENYL}-N' -(5-METHYL-3-ISOXAZOLYL)UREA SALT IN CRYSTALLINE FORM	:

PETITION TO MAKE SPECIAL UNDER 37 C.F.R. 1.102(D)

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

Applicants hereby submit this Petition To Make Special under 37 C.F.R. 1.102(d), and MPEP 708.02, part X, requesting that the present application be subject to expedited examination on the basis that the claimed invention relates to the treatment of cancer. In order to facilitate accelerated examination, Applicants are filing concurrently herewith a Preliminary Amendment limiting the claims to a most preferred embodiment of the present invention.

How the Present Invention Relates to Treatment of Cancer,

including a cancer common in HIV/AIDS patients

As noted in the specification at page 3, lines 6-10, the crystal of a salt according to the present invention is useful for the therapy of tumors, and Kaposi's sarcoma. Both of these are forms of cancer, with the latter, Kaposi's sarcoma, being a common form of cancer

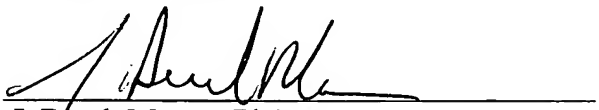
encountered by those afflicted with HIV/AIDS. In particular, as noted at page 33, beginning at line 20, the present invention compound N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea has tumor enhancement inhibitory activity in vivo (Pharmacological Test Examples 2, 3, and 4 in WO02/88110). Further, this compound inhibits in vitro the autophosphorylation activity in human KDR intracellular regions caused by stimulation of NIH3T3 cells, which can stably express human KDR, with VEGF (vascular endothelial growth factor) (Pharmacological Test Example 1 in WO 02/88110). Binding of VEGF to KDR, which is present as a receptor of VEGF on cell membranes, causes activation of MAPK (mitogen-activated protein kinase) and the like through autophosphorylation of KDR intracellular regions by tyrosine kinase (Shibuya M, Ito N, Claesson-Welsh L., in Curr. Topics Microbiol Immunol., 237; 59-83 (1999); Abedi, H. and Zachary, I., J. Biol. Chem., 272, 15442-15451 (1997)). The activation of MAPK is known to play an important role in the growth of vascular endothelial cells in angiogenesis (Merenmies, J. et al., Cell Growth & Differ., 83-10 (1997); and Ferrara, N. and Davis-Smyth, T., Endocr. Rev., 18, 4-25 (1997)). Therefore, the above compound has angiogenesis inhibitory activity. It is known that angiogenesis at pathologic sites is deeply involved mainly in several different diseases, such as tumors, and Kaposi's sacrcoma, (as well as diabetic retinopathy, chronic rheumatism, psoriasis, and atherosclerosis), and in the metastasis of solid tumors (Folkman, J. Nature Med. 1: 27-31 (1995); Bicknell, R., Harris, A. L. Curr. Opin. Oncol. 8: 60-65 (1996)). The present inventors have found that the salt forms of the subject compound, particularly the hydrochloride salts, provide distinct advantages in the oral administration and treatment of these diseases. Accordingly, the present invention falls within the definition provided for in MPEP 708.02, part X for treating cancer, and thus the present application should be Made Special for expedited examination.

Application No. 10/532,104
Inventor: Naoki MATSUNAGA, et al.

The undersigned requests that the present application be Made Special and that expedited examination be performed at the earliest possible date. Early notice of the granting of the present petition is respectfully requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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